REMARKS

Claims 1 and 3-7 were rejected and remain pending. In addition, claims 4-7 have been amended herein. For example, claims 4-6 have been amended to replace the word "mammal" with the word "mouse." Claim 7 has been amended herein to recite that the mouse comprises somatic and germ cells that are heterozygous for a disrupted IEX-1 sequence and to recite that the mouse homozygous for the disrupted IEX-1 sequence lacks expression of an IEX-1 polypeptide. Applicants' specification fully supports these amendments. For example, page 3, lines 3-6 disclose homozygous and heterozygous animals that can be used to obtain colonies of animals that are homozygous knockout, heterozygous, or wild-type. Thus, no new matter has been added.

In light of these amendments and the following remarks, Applicants respectfully request reconsideration and allowance of claims 1 and 3-7.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 4-6 and 7 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner stated that claims 4-6 lack antecedent basis for the term "mammal." In addition, the Examiner stated that the phrase "and lacks expression of an IEX-1 polypeptide" in claim 7 is unclear because it is not clear whether the phrase refers to the control mouse or to the homozygous IEX-1 disrupted mouse.

Claims 4-6 have been amended herein to replace the word "mammal" with the word "mouse." In addition, claim 7 has been amended herein to recite that the mouse homozygous for the disrupted IEX-1 sequence lacks expression of an IEX-1 polypeptide. Thus, claims 4-7 as amended are clear and unambiguous.

In light of the above, Applicants respectfully request withdrawal of the rejection of claims 4-7 under 35 U.S.C. § 112, second paragraph.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner maintained the rejection of claims 1 and 3-7 under 35 U.S.C. § 112, first paragraph. Applicants note that claims 4-6 have been amended herein to replace the word "mammal" with the word "mouse." In addition, claim 7 has been amended herein to recite that the mouse comprises somatic and germ cells that are heterozygous for a disrupted IEX-1 sequence. Applicants' specification fully enables present claims 1 and 3-7.

With respect to the Examiner's point bridging pages 4 and 5 of the Official Action mailed October 12, 2005, Applicants respectfully submit that a person having ordinary skill in the art reading Applicants' specification would not have needed undue experimentation to make and use the presently claimed invention. In fact, a person having ordinary skill in the art would have been able to use any one of many standard knock-out techniques to disrupt the expression of a polypeptide in a mouse. While making transgenic mice that over-express a particular gene to obtain a particular phenotype may be unpredictable in certain cases, making the presently claimed mice, which contain a disrupted IEX-1 sequence and lack expression of an IEX-1 polypeptide (when homozygous), certainly is not so unpredictable as to require undue experimentation whether removing exons from the beginning, middle, or end of the gene or whether inserting a sequence anywhere along the gene. Thus, Applicants' specification fully enables the presently claimed invention.

In light of the above, Applicants respectfully request withdrawal of the rejections of claims 1 and 3-7 under 35 U.S.C. § 112, first paragraph.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 1 and 3-7 under 35 U.S.C. § 103(a) as being unpatentable over the Lehoux and Tedgui reference (*Cir. Res.*, 93:1139-1411 (2003)) in view of Capecchi (*Trends in Genetics*, 5:70-76 (1989)).

Applicants respectfully disagree. Claims 1 and 3-6 recite a mouse whose somatic and germ cells comprise a disrupted IEX-1 sequence with the disruption resulting in the mouse

having a level of blood pressure that is higher than the level observed in a control mouse lacking the disruption. Claim 7 recites a mouse comprising somatic and germ cells that are heterozygous for a disrupted IEX-1 sequence, wherein a mouse homozygous for the disrupted IEX-1 sequence has a level of blood pressure that is higher than the level observed in a control mouse not homozygous for the disrupted IEX-1 sequence. Nowhere does the combination of cited references suggest that a person having ordinary skill in the art should make the presently claimed mice. For example, at no point does the combination of cited reference suggest making a mouse homozygous or heterozygous for the recited disrupted IEX-1 sequence that results in a homozygous mouse having a level of blood pressure that is higher than the level observed in a control mouse lacking the disruption. Thus, the present claims are not obvious.

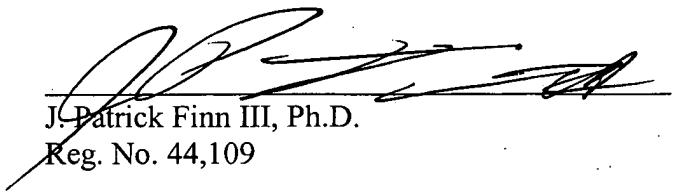
In light of the above, Applicants respectfully request withdrawal of the rejections of claims 1 and 3-7 under 35 U.S.C. § 103(a).

CONCLUSION

Applicants submit that claims 1 and 3-7 are in condition for allowance, which action is respectfully requested. The Examiner is invited to telephone Applicants' attorney if such would further prosecution. Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: February 7, 2006



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